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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,788	11/08/2001	Laurel J. Gershwin	023070-121000US	3215

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EXAMINER

GRUN, JAMES LESLIE

ART UNIT PAPER NUMBER

1641

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/052,788

Applicant(s)

GERSHWIN ET AL.

Examiner

James L. Grun

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 August 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-47 is/are pending in the application.
- 4a) Of the above claim(s) 1-9, 13, 16, 25 and 28-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-12, 14, 15, 17-24, 26, 27 and 47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-47 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 November 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>05/23/2002</u> . | 6) <input type="checkbox"/> Other: _____ |

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Applicant's election with traverse of Group II, claims 10-28 and 47, and the further election with traverse of the species SEQ ID NO: 5 in the paper filed 01 August 2005 are acknowledged. The traversal is on the ground(s) that it would not be unduly burdensome to search: the inventions of Groups III and IV with that of elected Group II because the inventions of Groups III and IV use the same proteins as Group II and should be examined together; and that SEQ ID NOs: 1-6 should be examined together because they are derived from the same protein. These are not found persuasive because the explanations of different processes, classifications, and fields of search made in the restriction requirement of record are sufficient to provide a *prima facie* showing of a serious burden upon the examiner and because peptides having different amino acid sequences and their uses are patentably distinct inventions. However, the examination of SEQ ID NOs: 1, 2, 4, and 5 together was not found burdensome by the examiner and these species have been rejoined for examination herein. Claims 1-9 and 29-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no (allowable) generic or linking claim. Claims 13, 16, 25, and 28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no (allowable) generic or linking claim. Claims 10-12, 14, 15, 17-24, 26, 27, and 47 are under active examination.

The requirement is still deemed proper and is therefore made FINAL.

The disclosure is objected to because of the following informalities: the imbedded hyperlink on page 10 is an impermissible incorporation by reference of the information on the

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referenced web page and deletion of elements which make it active, including deletion of "http://," is required. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 10-12, 14, 15, 17-24, 26, 27, and 47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to antibodies which specifically bind or which are elicited to polypeptides having at least 80% sequence identity with a particular disclosed sequence. The claims do not require that the antibodies or polypeptides possess any particular biological activity other than binding, nor any particular conserved structure, or other disclosed distinguishing feature(s). Thus, the claims are drawn to a genus of antibodies of unknown

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structure and properties that bind to a genus of polypeptides that are defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity that the antibodies bind. There is not even identification of any particular portion of the structure that must be conserved in the peptides or the antibodies. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, nor the antibodies which bind thereto, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of

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isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement that defines a genus of molecules by only their functional activity does not provide an adequate written description of the genus. The court indicated that although applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only antibodies binding to or elicited with the isolated polypeptides comprising the amino acid sequences set forth in SEQ ID NO: 1, 2, 4, or 5, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115). However, in view of the guidance in the instant specification to antibodies elicited to a single species, SEQ ID NO: 5, which function for the specific identification of native IgE in a sample as intended by applicant, the amount of experimentation required to determine functional structures or modifications for other usable species would also be undue. It is notoriously old and well known in the art that even single amino acid changes to a peptide epitope can have significant effects upon the binding

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of antibodies thereto. Even “conservative” substitutions with regard to protein structure or biochemistry may have unknown, unpredictable, and significant effects on the immunoreactivity of such a modified peptide compared to the unmodified peptide, particularly when the relevant epitope(s) is(are) unknown and this(these) epitope(s) has(have) the potential for being unpredictably functionally altered by **any** substitution. Not knowing, absent further experimentation, which modifications function and which do not, when, as set forth above, even a single change of an encoded amino acid can unpredictably affect structure and function, leads to one having no predictability or expectation of success for the function of any given modification. Such random experimentation to identify at a later time what structure or fragment or modification is or is not functional and is embraced by applicant’s claims is undue experimentation. Furthermore, very different structures may be found on antibodies with the same specificity. For example, very different variable heavy (V_H) chains can combine with the same variable light (V_L) chain to produce antibody binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_L sequences to produce antibodies with very similar properties. These observations indicate that divergent variable region sequences, both in and out of complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Conversely, similar structure may be found on antibodies having different specificities. Note that an enabling disclosure for the preparation and use of only a few analogs of a product does not enable all possible analogs where the characteristics of the analogs are unpredictable. See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* (18 USPQ 2d 1027 (CAFC 1991)).

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Therefore, only antibodies binding to or elicited with the isolated peptide comprising the amino acid sequence set forth in SEQ ID NO: 5, but not the full breadth of the claims meet the enablement provision of 35 U.S.C. §112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-24, 26, and 27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 22-24, 26, and 27, "the process" lacks antecedent basis.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-12, 14, 15, 17-19, 22-24, 26, 27, and 47 are rejected under 35 U.S.C. § 102(b) as being anticipated by Watson et al. (Vet. Allergy Clin. Immunol. 5: 135, 1997).

Watson et al. teach a population of antibodies elicited to a recombinant protein comprising the equine IgE sequences as instantly recited. Inherently, the population contained antibodies binding to any and every of the immunogenic epitopes in the protein. The antibodies were indirectly labeled with an enzyme for detection.

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Claims 10-12, 14, 15, 17, 18, 20, 22-24, 26, 27, and 47 rejected under 35 U.S.C. § 102(b) as being anticipated by Halliwell et al. (Curr. Eye Res. 4: 1023, 1985) in light of Watson et al. (Vet. Allergy Clin. Immunol. 5: 135, 1997) or the instant disclosure.

Halliwell et al. teach a population of antibodies elicited to an isolated protein comprising, in light of Watson et al. (Vet. Allergy Clin. Immunol. 5: 135, 1997) or the instant disclosure, the sequences as instantly recited. Inherently, the population contained antibodies binding to any and every of the immunogenic epitopes in the protein. The antibodies were directly labeled with radioactive iodine for detection

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

(c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 10-12, 14, 15, 17-24, 26, 27, and 47 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Marti et al. (Vet. Immunol. Immunopathol. 59: 253, 1997), Griot-Wenk et al. (Vet. Immunol. Immunopathol. 75: 59, 2000), Watson et al. (Vet. Allergy Clin. Immunol. 5: 135, 1997), and Lerner et al. (EP 0,044,710).

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Marti et al. teach the elicitation of antibodies to a recombinant fragment of equine IgE heavy chain comprising the CH3 and CH4 domains. Griot-Wenk et al. teach the elicitation of antibodies to a recombinant fragment of equine IgE heavy chain comprising the CH2 domain. The teachings of Watson et al. are as set forth above. Combined, the references teach the elicitation of anti-equine IgE antibodies to a variety of fragments thereof, but do not teach fragments smaller than a domain.

Lerner et al (EP 0,044,710) teach a method to design and produce specific antigen to produce antibodies for any desired purpose (page 9) including diagnostic assays (page 11). Lerner et al further enumerate the necessary steps (pages 12-13): determine the amino acid sequence of all or part of a peptide region of interest from a natural antigen; predict regions of the peptide which are potential epitopes; prepare a synthetic epitope-containing peptide which immunologically duplicates the potential epitope of the natural antigen; couple the synthetic epitope-containing peptide to a pharmaceutically acceptable carrier, such as keyhole limpet hemocyanin (KLH) (e.g. pages 23 or 32); and, inject the epitope-containing peptide into a host to produce antibodies. Cys amino acid residues can be added to an epitope-containing peptide to facilitate coupling (e.g. page 22 and Fig. 10). Epitope-containing peptides may be linked together as homopolymers or copolymers (e.g. page 59).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have provided peptides corresponding to, and/or antibodies specific for, any of a variety of regions of the known sequences of the equine IgE protein for use in any of Marti et al., Griot-Wenk et al., or Watson et al. because, as taught therein, the equine IgE proteins are of unquestioned clinical interest, the generic uses of antibodies elicited to and

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specific for equine IgE polypeptides in the immunoassays of the references for detection of equine IgE are taught, it is conventional in the art to provide peptides of a sequenced protein coupled to a carrier and to elicit either polyclonal or monoclonal antibodies thereto for a variety of uses as taught in any of Marti et al., Griot-Wenk et al., Watson et al., or Lerner et al., and one of ordinary skill in the art would have had an extremely reasonable expectation of success in achieving the expected result, i.e. generating antibodies, either polyclonal or monoclonal antibodies specifically reactive with specific peptide epitopes in equine IgE proteins, providing and using synthetic or recombinant peptide immunogens derived from the sequences of the equine IgE proteins, taught in Marti et al., Griot-Wenk et al., or Watson et al., in conjunction with notoriously old and well known conventional techniques as taught by any of Marti et al., Griot-Wenk et al., Watson et al., or Lerner et al. See Ex parte Erlich (3 USPQ2d 1011 (BPAI 1987)). It would have been further obvious to have generated hybridomas producing monoclonal antibodies, which could be isolated therefrom, in order to provide a potentially unlimited source of homogeneous reagent. It would have been further obvious to have provided any of the conventional detectable labels on the antibodies as such labeling is conventional in the art for, inter alia, detection of antibody binding as taught in Marti et al., Griot-Wenk et al., or Watson et al. Moreover, it would have been obvious to have formulated the reagents of Marti et al., Griot-Wenk et al., or Watson et al., as modified, into a kit since that is conventional for convenience, economy, and reproducibility.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



James L. Grun, Ph.D.
September 16, 2005



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